

What is claimed is:

1. An array based molecular descriptor device for interacting with a specific ligand molecule or structure comprising:

an array of electronic microlocations,

capture intermolecular ligand binding components coupled to the microlocations, the intermolecular ligand binding components including a capture programmable pairing component and a ligand binding component, the capture programmable pairing component being the same at the various microlocations and the ligand binding component being different at the various microlocations, and

supramolecular complexes formed at ~~at~~ least certain of the microlocations, the supramolecular complex comprising said capture intermolecular ligand binding component, a first programmable pairing component complementary to, at least, a portion of the capture programmable pairing component, including a ligand binding component, and a second programmable pairing component complementary to the capture programmable pairing component and having a ligand binding component, and a specific ligand molecule or structure, such that upon binding of the specific ligand molecule or structure a specific supermolecular complex forms, via the pairing of the specific first programmable pairing component, the second programmable pairing component and the capture programmable pairing component.

2. The array based device of claim 1 wherein the programmable pairing components include p-RNA.

3. The array based device of claim 1 wherein the programmable pairing component includes CNAs.

4. The array based device of claim 1 wherein the programmable pairing component includes a composite system.

5. The array based device system of claim 4 wherein the composite system includes both p-RNA and DNA.

6. The array based device of claim 1 wherein the programmable pairing component includes nucleic acid.

10 7. The array based device of claim 6 wherein the nucleic acid is DNA.

8. The array based device of claim 6 wherein the nucleic acid is RNA.

15 9. The array based device of claim 1 wherein the electronic microarray has independently controllable electronic microlocations.

10. The array based device of claim 1 wherein the ligand binding components include peptides.

20 11. The array based device of claim 10 wherein the ligand binding components comprise peptide sequences.

25 12. The array based device of claim 11 wherein the peptide sequences are hexamer peptide sequences.

13. The array based device of claim 1 wherein the ligand binding component includes an amino acid.

30 14. The array based device of claim 1 wherein the ligand binding component includes an antibody.

15. The array based device of claim 1 wherein the ligand binding component includes a protein.

5 16. The array based device of claim 1 wherein the ligand binding component includes an enzyme.

17. The array based device of claim 1 wherein the ligand binding component includes a metal chelator.

10

18. The array based device of claim 1 wherein the ligand binding components are selected from a combinatorial library.

a 19. The array ^{based}~~base~~ device of claim 1 wherein the ligand binding components
15 comprise a combination of various ligand binding components.

20. The array based device of claim 19 wherein one ligand binding component comprises a peptide ligand binding component and another ligand binding component comprises a metal chelator.

20

21. The array based device of claim 1 wherein the specific ligand molecule comprises a small molecule.

22. The array based device of claim 21 wherein the small molecule comprises
25 a drug.

23. The array based device of claim 21 wherein the small molecule comprises a metabolite.

24. The array based device of claim 21 wherein the small molecule comprises a metal ion.

5 25. The array based device of claim 21 wherein the small molecule comprises a peptide.

26. The array based device of claim 1 wherein the specific molecule comprises a large molecule.

10 27. The array based device of claim 26 wherein the large molecule comprises a protein.

15 28. The array based device of claim 26 wherein the large molecule comprises an enzyme.

29. The array based device of claim 26 wherein the large molecule comprises an antibody.

20 30. The array based device of claim 26 wherein the specific structure comprises an organelle.

31. The array based device of claim 26 wherein the specific structure comprises a cell.

25 32. The array based device of claim 1 further including an electronic stringency system.

30 33. The array based device of claim 32 wherein the electronic stringency system includes a perturbation system.

34. The array based device of claim 1 further including an illumination source.

35. The array based device of claim 34 further including a detector.

5 36. The array based device of claim 1 further including an analysis system.

37. The array based device of claim 1 further including a display.

10 38. The array based device of claim 1 further including an electronic control system.

39. The array based device of claim 1 further including a data processing system.

15 40. An array based molecular descriptor device for interacting with a specific ligand molecule or structure comprising:

an array of electronic microlocations,

intermolecular ligand binding components coupled at the microlocations, the intermolecular ligand components including a p-RNA capture programmable pairing component and a ligand binding component, the capture p-RNA programmable pairing component being the same at the various microlocations, and the peptide ligand binding component being different at the various microlocations, and

20
25
30
supermolecular complexes formed at ~~at~~ least certain of the microlocations, the supermolecular complex comprising said capture intermolecular ligand binding structure, a first p-RNA programmable pairing component complementary to at least a portion of the capture programmable pairing component, including a peptide ligand binding component, and a second p-RNA programmable pairing component complementary to the capture programmable pairing component and

5 having a peptide ligand binding component, and a specific ligand molecule or structure, such that in the presence of the specific ligand molecule or structure a specific supermolecular structure forms via the selective binding by the specific first programmable pairing component, the second programmable pairing component and the capture programmable pairing component.

41. A method for the combinatorial selection of supermolecular complexes on an electronic array based device comprising the steps of:

10 providing capture intermolecular ligand binding structures at a plurality of sites on the array, each capture intermolecular ligand binding structure having a common capture programmable pairing component and a different ligand binding component,

15 providing complementary intermolecular ligand binding structures to the device, having a programmable pairing component which is complementary to the capture programmable pairing component and includes a ligand binding component, and a specific ligand molecule or structure,

20 setting the stringency conditions on the device to effect supermolecular complex formation, and

 detecting the microlocations at which supermolecular complexes have been formed.

25 42. The method of claim 41 wherein the stringency conditions include electronic stringency.

 43. The method of claim 42 wherein the electronic stringency conditions include electronic perturbation.

44. The method of claim 41 wherein the stringency conditions include conventional stringency conditions.

5 45. The method of claim 44 wherein the stringency conditions include temperature.

46. The method of claim 44 wherein the stringency conditions include pH.

10 47. The method of claim 44 wherein the stringency conditions include ionic strength.

48. The method of claim 44 wherein the stringency conditions include chemical agents.

15 49. The method of claim 44 further including the step of determining the ligand binding components involved in a given supermolecular complex.

20 50. The method of claim 44 wherein the identity of the ligand binding components is used in the selection of ligand binding components for a second array.

51. The method of claim 44 wherein the identity of the ligand binding components is utilized to form synthetic antibodies.

25 52. The method of claim 44 wherein the identity of the ligand binding components is utilized to form new affinity reagents.

53. The method of claim 44 wherein the identity of the ligand binding components is utilized to form synthetic catalysis/enzymes.

54. The method of claim 44 wherein the identity of the ligand binding components is utilized to form new metal chelate structures.

55. A method for determining an expected biological response of a test
5 substrate (molecule) comprising the steps of:

providing a molecular descriptor array on which supramolecular complexes may form at definable locations,

10 applying at least one known substrate, monitoring the response of the known substrate on the molecular descriptor array and developing a response profile therefrom,

applying a test substrate (molecule) to the molecular descriptor array and monitoring the response thereto, and

15 analyzing the response of the test substrate (molecule) on the molecular descriptor array in relationship to the response from the known substrate so as to determine the expected biological response of the test substrate.

56. A method for drug discovery comprising the steps of:

20 providing a molecular descriptor array having a plurality of definable locations,

25 providing a drug to the molecular descriptor array, and monitoring the response of the molecular descriptor array to the drug, thereby developing a response profile for the drug,

subsequently providing in series related compounds to the molecular descriptor array, monitoring the response of the molecular descriptor array to the related compounds, thereby developing further response profiles for the related compounds, and

30 providing a test compound to the molecular descriptor array, monitoring the response of the molecular descriptor arrays to the test compound and analyzing the response of the test compound relative to the

response profiles for the drug and related compounds so as to predict expected response of the test compound.

60. The method of claim 56 wherein the related compounds are toxins.

61. A method for evolving an improved molecular descriptor array comprising the steps of:

providing a first molecular descriptor array,

applying a specific ligand molecule or structure to the first molecular descriptor array, monitoring the response to the specific ligand molecule or structure on the molecular descriptor array, and identifying supermolecular structures and their specific ligand binding components, and

providing a second library of ligand binding components, the components of the library being selected at least in part based upon the identified ligand binding components from the first molecular descriptor array interaction, and providing a second molecular descriptor array utilizing the second combinatorial library.

62. The method of claim 61 wherein the libraries include peptide sequences.

63. The method of claim 61 wherein the second library includes peptide sequences which are longer than the peptide sequences in the first library.

64. The method of claim 61 wherein the second library includes other amino acids not included in the first library.

5 65. The method of claim 61 wherein the second library comprises a subset of the first library.

66. A method for formation of supermolecular complexes on an array, comprising the steps of:

providing an array of microlocations,

10 providing capture intermolecular ligand binding structures at the microlocations, the capture intermolecular binding structures having capture programmable pairing components which are common to the various microlocations and ligand binding components which vary from microlocation to microlocation,

15 contacting the array with a solution containing intermolecular ligand binding components a and intermolecular ligand binding components b, under conditions where the programmable pairing components of the intermolecular binding structures a and b are in dynamic equilibrium with the pairing components of the capture intermolecular ligand binding structure,

20 introducing a specific ligand molecule or structure, and

forming supermolecular complexes at certain of the microlocations.

25 67. The method of claim 66 wherein the dynamic equilibrium conditions are at or near the melting temperature of the supermolecular complex comprising the capture intermolecular ligand binding structure and the intermolecular ligand binding structures a and b.

68. The method of claim 66 wherein the dynamic equilibrium conditions are at 5°C or less than the melting temperature.

5 69. The method of claim 66 wherein the array is an active microelectronic array.

70. The method of claim 66 wherein the dynamic equilibrium conditions include electronic stringency conditions.

10 71. The method of claim 66 wherein the electronic stringency conditions include electronic perturbation.

72. A method for the formation of supermolecular complexes comprising the steps of:

15 providing in a solution phase a specific ligand molecule or structure, and intermolecular ligand binding structure a and an intermolecular ligand binding structure b under conditions to form a dimer complex of the specific ligand molecule or structure, / intermolecular ligand binding structure a and intermolecular ligand binding structure b, and

20 contacting the dimer complex with an array of capture intermolecular ligand binding structures, each capture intermolecular ligand binding structure having a common capture programmable pairing component and a different ligand binding component, under conditions so
25 as to form a supermolecular structure consisting of a dimer complex and a capture intermolecular ligand binding component.

73. The method of claim 72 wherein the formation of the dimer complex is done separate from the array.

30

74. The method of claim 72 wherein the dimer complexes are formed in solution on the array.

75. The method of claim 72 wherein the array is an electronic array.

76. The method of claim 72 wherein the electronic array is placed in a repulsive condition to the components during the formation of the dimer complexes.

77. A method for the formation of supermolecular structures on an electronic microarray comprising the steps of:

providing an array of microlocations, each microlocation including a capture intermolecular ligand binding structures, the intermolecular ligand binding structure having a common programmable pairing component and varying ligand binding components,

contacting the array with intermolecular ligand binding structures a and intermolecular binding structures b having programmable pairing components adapted to pair with the capture programmable pairing component, and ligand binding components,

introducing the specific ligand molecule or structure, and

varying the stringency conditions to determine the specific supermolecular complex locations on the array.

78. The method of claim 77 wherein the stringency conditions include electronic stringency conditions.

79. The method of claim 77 wherein the electronic stringency conditions include electronic perturbation.

80. A method for performing multiple immunological reactions on a microelectronic array device comprising the steps of:

providing a plurality of microelectronic sites, each site having a programmable pairing component couple thereto, the programmable pairing components varying from site to site,

5 providing a plurality of different types of antibodies, each type of antibody being labeled with a different programmable pairing component, the different programmable pairing components being complementary to the programmable pairing components coupled to the microelectronic sites,

providing an antigen,

10 reacting the antigen and the plurality of labeled, different types of antibodies with the programmable pairing components at the microelectronic sites,

interacting the programmable pairing component and the complement programmable pairing, and

15 determining the sites at which an antibody coupled to the antigen coupled to the complementary programmable pairing component is present.

81. The method of claim 80 wherein the antigen and plurality of labeled, different types of antibodies are provided together in a homogeneous format.

20 82. The method of claim 80 wherein the programmable pairing component and the complement to the programmable pairing component are p-RNA.

83. A device for the formation and detection of supramolecular complexes comprising:

25 an attachment surface, the attachment surface being located in a variable electronic environment,

a molecular recognition system, including at least a first and a second molecular recognition component, at least the first component being attached to the surface,

a separate molecular species bound to the molecular recognition system,
and

a third structure for formation of a supramolecular complex with the
separate molecular species.

5

84. The device for the formation and detection of supramolecular complexes
of claim 83 wherein the molecular recognition system comprises a pairing system.

10

85. The device for the formation and detection of supramolecular complexes
of claim 84 wherein the pairing system is a complementary pairing system.

86. The device for the formation and detection of supramolecular complexes
of claim 85 wherein the pairing system is a complementary and coded pairing system.

15

87. The device for the formation and detection of supramolecular complexes
of claim 86 wherein the complementary pairing system is a p-RNA pairing system.

20

88. The device for the formation and detection of supramolecular complexes
of claim 83 wherein the separate molecular species includes a peptide.

89. The device for the formation and detection of supramolecular complexes
of claim 88 wherein the separate molecular species comprises a peptide sequence.

25

90. The device for the formation and detection of supramolecular complexes
of claim 88 wherein the separate molecule species comprises an antibody.

91. The device for the formation and detection of supramolecular complexes
of claim 88 wherein the separate molecule species comprises an antibody fragment.

92. The device for the formation and detection of supramolecular complexes of claim 88 wherein the separate molecule species comprises a specific binding protein.

5 93. The device for the formation and detection of supramolecular complexes of claim 88 wherein the separate molecule species comprises a specific biological binding site.

10 94. The device for the formation and detection of supramolecular complexes of claim 93 wherein the physiological binding site is an isolated biological binding site.

15 95. The device for the formation and detection of supramolecular complexes of claim 93 wherein the physiological binding site is a cloned biological binding site.

20 96. The device for the formation and detection of supramolecular complexes of claim 93 wherein the physiological binding site is a mimicry biological binding site.

25 97. The device for the formation and detection of supramolecular complexes of claim 93 wherein the ^{physiological} ~~physiological~~ binding site is a fused biological binding site.

30 98. The device for the formation and detection of supramolecular complexes of claim 83 wherein the separate molecular species are from a combinatorial library.

99. The device for the formation and detection of supramolecular complexes of claim 98 wherein the library includes more than one species.

100. The device for the formation and detection of supramolecular complexes of claim 98 wherein the library includes at least 10 species.

101. The device for the formation and detection of supramolecular complexes of claim 98 wherein the library includes at least 100 species.

102. The device for the formation and detection of supramolecular complexes of claim 98 wherein the library includes at least 1000 species.

5 103. The device for the formation and detection of supramolecular complexes of claim 98 wherein the library includes at least 10,000 species.

104. The device for the formation and detection of supramolecular complexes of claim 98 wherein the library is a sublibrary aggregated to form a higher order library.

10

105. The device for the formation and detection of supramolecular complexes of claim 83 wherein a single separate molecular species is bound to the molecular recognition system.

15

106. The device for the formation and detection of supramolecular complexes of claim 105 wherein a cooperative ensemble of molecular species are bound to the molecular recognition system.

20

107. The device for the formation and detection of supramolecular complexes of claim 106 wherein there are two molecular species (a diad).

108. The device for the formation and detection of supramolecular complexes of claim 106 wherein there are three molecular species (a triad).

25

109. The device for the formation and detection of supramolecular complexes of claim 98 wherein the components of the library identify specific molecular properties.

110. The device for the formation and detection of supramolecular complexes of claim 98 wherein the components of the library identify specific chemical properties.

30

111. The device for the formation and detection of supramolecular complexes of claim 109 wherein the property is binding.

5 112. The device for the formation and detection of supramolecular complexes of claim 109 wherein the property is molecular recognition.

113. The device for the formation and detection of supramolecular complexes of claim 109 wherein the property is chemical.

10 114. The device for the formation and detection of supramolecular complexes of claim 109 wherein the property is physical activity.

15 115. The device for the formation and detection of supramolecular complexes of claim 83 wherein the separate molecular species is covalently bound to the molecular recognition system.

20 116. The device for the formation and detection of supramolecular complexes of claim 83 wherein the separate molecular species is supermolecularly bound to the molecular recognition system.

117. The device for the formation and detection of supramolecular complexes of claim 116 wherein the supramolecular binding include a strepdauidin/biotin interaction.

25 118. The device for the formation and detection of supramolecular complexes of claim 83 wherein the separate molecular species is bound to both the first and the second molecular recognition component.

30 119. The device for the formation and detection of supramolecular complexes of claim 83 wherein the supramolecular complex includes covalent binding.

120. The device for the formation and detection of supramolecular complexes of claim 83 wherein the supramolecular complex includes supramolecular binding.

5 121. The device for the formation and detection of supramolecular complexes of claim 98 wherein there are n species of the types and the number of variations is b^n .

122. The device for the formation and detection of supramolecular complexes of claim 83 further including a detector.

10

123. The device for the formation and detection of supramolecular complexes of claim 122 where the detector detects the presence of a supramolecular complex.

15

124. The device for the formation and detection of supramolecular complexes of claim 122 where the detector detects a property respecting the assembly of the supramolecular complex.

20

125. The device for the formation and detection of supramolecular complexes of claim 122 where the detector detects a property respecting the disassembly of the supramolecular complex.

25

126. The device for the formation and detection of supramolecular complexes of claim 125 wherein the detector detects a property respecting the disassembly of the supramolecular complex includes the off-rate.

127. The device for the formation and detection of supramolecular complexes of claim 122 wherein the detection includes a competitive binding format.

30

128. The device for the formation and detection of supramolecular complexes of claim 122 wherein the detection includes a sandwich format.

129. The device for the formation and detection of supramolecular complexes of claim 83 wherein a plurality of physically distinct sites each comprising an attachment surface being located in a variable electronic environment.

5

130. The device for the formation and detection of supramolecular complexes of claim 129 wherein each site has a common first molecular recognition component.

a 10 131. The device for the formation and detection of supramolecular complexes of claim 129 wherein each site has ^{different}~~different~~ components.

a 15 132. The device for the formation and detection of supramolecular complexes of claim 83 wherein at least one of the molecular recognition components, the separate molecular species/or the supramolecular complex is labeled.

133. The device for the formation and detection of supramolecular complexes of claim 132 wherein the label comprises a fluorescent label.

20 134. The device for the formation and detection of supramolecular complexes of claim 83 comprising a diagnostic device.

25 135. The device for the formation and detection of supramolecular complexes of claim 134 wherein the diagnostic device tests materials from the group consisting of: blood, tissue, feces, cells, cell compartments, and cell factions.

30 136. A method for forming supramolecular structures in an exponential library by aggregation of sublibraries (ELIAS), the improvement comprising subjecting at least certain of the components for formation of a supramolecular complex to electronic stringency.

Year	1950	1951	1952	1953	1954	1955	1956	1957	1958	1959	1960	1961	1962	1963	1964	1965	1966	1967	1968	1969	1970	1971	1972	1973	1974	1975	1976	1977	1978	1979	1980	1981	1982	1983	1984	1985	1986	1987	1988	1989	1990	1991	1992	1993	1994	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022	2023	2024	2025	2026	2027	2028	2029	2030	2031	2032	2033	2034	2035	2036	2037	2038	2039	2040	2041	2042	2043	2044	2045	2046	2047	2048	2049	2050	2051	2052	2053	2054	2055	2056	2057	2058	2059	2060	2061	2062	2063	2064	2065	2066	2067	2068	2069	2070	2071	2072	2073	2074	2075	2076	2077	2078	2079	2080	2081	2082	2083	2084	2085	2086	2087	2088	2089	2090	2091	2092	2093	2094	2095	2096	2097	2098	2099	2100
1950	1951	1952	1953	1954	1955	1956	1957	1958	1959	1960	1961	1962	1963	1964	1965	1966	1967	1968	1969	1970	1971	1972	1973	1974	1975	1976	1977	1978	1979	1980	1981	1982	1983	1984	1985	1986	1987	1988	1989	1990	1991	1992	1993	1994	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022	2023	2024	2025	2026	2027	2028	2029	2030	2031	2032	2033	2034	2035	2036	2037	2038	2039	2040	2041	2042	2043	2044	2045	2046	2047	2048	2049	2050	2051	2052	2053	2054	2055	2056	2057	2058	2059	2060	2061	2062	2063	2064	2065	2066	2067	2068	2069	2070	2071	2072	2073	2074	2075	2076	2077	2078	2079	2080	2081	2082	2083	2084	2085	2086	2087	2088	2089	2090	2091	2092	2093	2094	2095	2096	2097	2098	2099	2100	